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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,354	12/12/2001	William Dall'Acqua	10271-027	2678

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,354	DALL'ACQUA ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-86* is/are pending in the application.

4a) Of the above claim(s) *1,5,6,9,13,17,21-57,59-68 and 70-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4, 7,8, 10-12,14-16,18-20,58,69 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-86 are pending.

2. Applicant's election with traverse of Group I, claims 1-4, 7-20, 58, 69 and 86 and substitution with tyrosine at position of 252 as a specific modification at specific position of modified IgG and antibody sequence of A4B4L1FR-S28R as specific antibody sequence in response to restriction Requirement filed on 1/29 /04 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the inventions must be both independent and distinct and that the search of Groups I-III together would not constitute a serious search burden on the examiner and that search of the claims of Group I would provide useful information for the claims of Group II and Group III. However, MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required.

Regarding applicant's comments about undue burden, the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria, indicates that inventions recognized divergent subject matter and that a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. All the above establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in the previous Office Action and above.

The requirement is still deemed proper and is therefore made FINAL.

The elected substitution with tyrosine at position of 252 as a specific modification at specific position of modified IgG is free of the prior art. The prior art search has been extended to include: (i) substitution with threonine at positions 254 and 256 as specific modification at specific position of modified IgG, and (ii) modified IgG which has the heavy chain variable domain and light chain variable domain of SYNAGIS^{R}.

Claims 5-6, 21-57, 59-68 and 70-85 (non-elected groups II –XV) and claims 1, 9, 13, 17, (non-elected species of elected group I) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 2-4, 7, 8, 10-12, 14-16, 18 –20, 58, 69 and 86 read on a modified IgG, a pharmaceutical composition and a kit comprising said modified IgG, wherein modification is substitution with tyrosine at position of 252 or substitution with threonine at positions 254 and 256, and modified IgG which has the heavy chain variable domain and light chain variable domain of SYNAGIS^R or A4B4L1FR-S28R under consideration in the instant application.

3. Applicant asserts that " a revised form PTO 1449" has been submitted with an application. It is noted however, that "a revised form PTO 1449" and the references cited in said form have not been found . Applicant is invited to resubmit said form and references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-4, 7-8,10-12, 14-16, 18, 19, 20 58, 69 and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 2-3 are indefinite and ambiguous in the recitation of "modification of IgG at position 251-256. Recitation of amino acid position from the first amino acid of a protein without providing SEQ ID NO for the protein is indefinite and ambiguous because different laboratories may have different numbering of the same protein.

B. Claim 20 is indefinite and ambiguous in the recitation of "A4B4l1FR-S28R" because its characteristics are not known. The use of " A4B4l1FR-S28R " as the sole means of identifying the claimed antibody renders the claim indefinite because " A4B4l1FR-S28R " is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct antibody.

C. Claim 19 contains the trademark name SYNAGIS^R. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or

trade name. In the present case, the trademark name is used to identify/describe antibody and, accordingly, the identification/description is indefinite.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

8. In claims 19 and 20 , it is apparent that SYNAGIS^{R} and A4B4L1FR-S28R are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit hybridoma producing SYNAGIS^{R} and A4B4L1FR-S28R. See 37 CFR 1.801-1.809.

With regards to SYNAGIS^{R} antibody.

The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample. The relationship between the applicant relying on a biological material and the commercial supplier is one factor that would be considered in determining whether the biological material was known and readily available. However, the mere fact that the biological material is commercially available only through the patent holder or the patent holder's agents or assigns shall not, by itself, justify a finding that the necessary material is not readily available, absent reason to believe that access to the biological material would later be improperly restricted. Moreover, the concepts of "known and readily available to the public" are considered to reflect a level of public accessibility to a necessary component of the invention disclosure that is consistent with the ability to make and use the invention. Neither concept alone is sufficient. A material may be known in the sense that its existence has been published, but is not available to those who wish to obtain that particular known biological material. Likewise, a biological material may be available in the sense that those having possession of it would make it available upon request, but no one has been informed of its existence (See MPEP 2404.01). The applicant did not make of record any of the facts and circumstances surrounding the access to SYNAGIS^{R} antibody at the time the invention was made.

With regards to A4B4L1FR-S28R antibody.

If the deposit have been made under the terms of the Budapest treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma producing A4B4L1FR-S28R have been deposited under the Budapest Treaty and that the hybridoma producing A4B4L1FR-S28R will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806 1.808 (a)(2) and MPEP 2410-2410.01.

If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in position to make such assurances, or statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met

Amendment of the specification to disclose the date of the deposit and complete name and address of the depository is required.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

Claims 2-4, 7, 8, 10 –12, 15, 16, 58 and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,277,375.

US Patent '375 teaches a modified human , humanized and non-human IgG comprising an IgG constant domain, wherein modified IgG has an increase half-life compared to the half-life of an IgG having the wild type IgG constant domain.(see entire document, Abstract in particular). US Patent '375 teaches that said modified IgG has higher affinity for the FcRn at pH 6.0 than at pH 7.4 (see column 2, lines 28-35 in particular). US patent '375 teaches the general method to make a modified IgG that has an increase half-life compared to the half-life of an IgG having the wild

type IgG constant domain. US Patent '375 teaches a specific positions and specific amino acids modifications in CH2 and CH3 domains that increases half life of said modified IgG , including substitution threonine at position 252 , threonine at position 254 and threonine at position 256(see column 3, line 25-50, column 4, lines 50-65 in particular). US Patent '375 teaches that production an modified IgG with increased in vivo half-life would be generally useful in treating various diseases (see overlapping columns 3-4 in particular) and that similar strategies are applicable to immunoglobulin-like domains of various molecules (see column 5, lines 25-45 in particular) . US Patent '375 teaches a pharmaceutical composition and kit comprising said modified IgG (see column 29, lines 29-35 in particular). US Patent '375 teaches an advantageous method for determining other residues important for catabolism control that can be modified by substitution to increase a half-life of a modify IgG (see column 4, lines 50-60 in particular).

The reference teaching anticipates the claimed invention.

10. Claims 3, 15, 19 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,277,375 in view of US Patent 6,572,856.

The teaching of US Patent '375 have been discussed, supra.

US Patent '375 does not explicitly teach human or humanized modified IgG which has the heavy chain variable domain and light chain variable domain of SYNAGIS^{R} , as claimed in claim 19, or specifically binds to an RSV antigen, as claimed in claim 86.

US Patent '856 teaches SYNAGIS^{R} antibody, which is a humanized anti-respiratory syncytial virus monoclonal antibody which specifically binds to an RSV antigen. (see entire document, Abstract and Column 10, line 49-55 in particular). US Patent '856 teaches that an effective strategies and methods for treating viral infection, including RSV comprises increasing persistence of said antibodies in circulation (see overlapping columns 2-3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '856 to those of US Patent '375 to obtain a claimed modified IgG which has the heavy chain variable domain and light chain variable domain of SYNAGIS^{R} , or specifically binds to an RSV antigen.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because increasing persistence of antibodies in circulation, for example modified IgG which has the heavy chain variable domain and light chain variable domain of SYNAGIS^{R} , or specifically binds to an RSV antigen would be beneficial for treatinf viral infection. This can be done by increasing half-life of IgG by modifying IgG by the method taught by US Patent '375. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles

or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. The prior art does not teach or suggest a modified IgG wherein amino acid substitution is a substitution with tyrosine or tryptophane at position 252.

13. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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